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January 5, 2000

Jane Henney, M.D. Commissioner
Dockets Management Branch HFA-305
Food and Drug Administration
5630 Fishers Lane, Room 1061
Rockville, MD 20852

RE: FDA's proposed rule: Suitability Determination for Donors of Human Cellular and Tissue Banked Products (Docker No. 97N-484S)

Dear Commissioner Henney:

I am writing to you as a corneal transplant surgeon and volunteer medical director for the Northeast Pennsylvania Lions Eye Bank in Allentown, PA about the food and drug administrations proposed rule: suitability determination for donors of human cellular and tissue banked products. I agree completely with the Eyebank Association of America's comments and have enclosed them with this letter. The EBAA has always been at the forefront setting stringent medical standards based on scientific literature. This proposed rule by the FDA has no scientific basis when applied to corneal tissue and could put undue costs on eye banks throughout the nation. I hope you agree with this and grant relief from the imposition of additional regulatory requirements established under this proposed rule for human eye tissue until the public health threat is founded.

Sincerely,

Alan Leahey M.D.

Alan B. Leahey, M.D.

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c Dick Rader

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[The FDA has been provided copies of EBAA's Medical Standards and supporting documents.]

The EBAA's Medical Standards are specific to banked human eye tissue, scientifically-based and developed to ensure safe transplantation. EBAA's Medical Standards are twice-yearly peer-reviewed and revised when necessary to ensure the practice of state-of-the-art safety procedures. Such standards and procedures are also reviewed annually by the American Academy of Ophthalmology. It should be noted that the EBAA was the first transplant organization to institute mandatory testing of transplant donors for the presence of HIV. The Association was among the first transplant organizations to institute mandatory testing and screening procedures for hepatitis B and C as testing became available.

FDA's Proposal:

FDA proposes to broadly regulate human tissue and requires most establishments to test for syphilis and screen for transmissible spongiform encephalopathies (TSE), including Creutzfeldt-Jakob disease (CJD); exceptions are made in certain limited situations. The proposal ignores the agency's statement on page 52713 of the Federal Register, which states that the risks of disease transmission vary by cellular and tissue-based product.

EBAA's Position:

The American corneal tissue supply is safe. No public health threat exists; there has been zero transmission of systemic-infectious disease in over 560,000 corneal transplants, for the last 13 consecutive years. The present regulatory system, consisting of current FDA regulation under Part 1270, the eye bank communities adherence to stringent community-specific and self-imposed standards, and protections afforded by the legal system in this country, is effective as noted by the community's safety history.

The proposed regulation places corneal transplant tissue under a generic and all inclusive regulatory framework not warranted by experience or scientific evidence. This proposed rulemaking, inclusive of all tissue, mimics the practice of defensive medicine -- "defensive rulemaking" -- where tests are ordered beyond the scope of practice parameters, are costly, and add no determined medical benefit. Generic and broad-based safety standards will undermine specific requirements that are peer-reviewed for the eye banking community. The adoption of FDA's broad regulatory approach may actually foster problems in a community that has experienced no transmission of systemic-infectious disease for over 13 years. These issues are specifically addressed later in this response.

The economic impact of the proposed rule is significantly understated. The requirements under the proposed rule would produce a cost with no related increase in safety. The burden of potentially paying a user fee in the future for this type of unnecessary oversight will further add to acquisition costs. Cost increases are not easily absorbed by the not-for-profit eye bank community. At some point, access will be impaired for no justifiable reason.

Corneal tissue destined for human transplant is not a manufactured device or drug, but is a living tissue with a very limited period of viability. The cornea must be recovered, evaluated, medically screened including serological testing for viral markers and provided for transplantation as soon as possible. Ideally, this occurs in one to two days after tissue recovery. Beyond five days, a cornea is unlikely to be acceptable to a U.S. surgeon. Unlike other human tissue, time is of the essence in screening and releasing corneal tissue in the effort to achieve the optimal surgical outcome for the patient/recipient. The FDA's proposed requirements under this rule will increase testing time with no proven benefit, thus pushing the acceptable time limit for transplantation, posing quality problems.

The American Corneal Tissue Supply is Safe:

Since the adoption of EBAA's Medical Standards in 1980, there have been only two reported cases of systemic disease transmission by corneal transplantation in over 850,000 corneal transplants in the United States. Both, cases of hepatitis B, occurred in the early 1980s prior to the development of hepatitis testing. As noted above, the EBAA was among the first transplant organizations to institute mandatory screening and testing procedures for hepatitis B. **With the advent of hepatitis B testing, there have been no cases of any systemic infectious disease transmission in over 560,000 U.S. corneal transplants. This record is testimony that the present self-regulatory approach is working. A 100% safety record cannot be improved.**

On the rare occasion when transmission of systemic infectious disease has occurred, the community has immediately responded, risen to the challenge, reviewed the case vis-à-vis relevant standards and available scientific knowledge, and adopted changes to prevent future occurrence. In sum, in emerging situations there is a mechanism to institute new eye bank community standards to safeguard the donor cornea pool.

EBAA medical standards require routine screening of donors for the following: active viral hepatitis, human immunodeficiency virus (HIV), or HIV seropositive donor, active viral encephalitis or encephalitis of unknown origin, Cruetzfeldt-Jacob Disease (CJD), and rabies. EBAA requires screening of donors for symptoms of transmissible spongiform encephalopathies (TSE) or CJD despite the fact that no known corneal recipients have contracted TSE or CJD in the last twenty-five years in the U.S. This fall, the EBAA convened a group of medical experts to further evaluate standards and procedures for safety relative to TSE and CJD concerns presented outside the United States. We believe this data is critical to determining appropriate eye banking practice. This model, a peer-reviewed scientific approach to public health concerns, is necessary to protect public health and ensure the integrity of the eye banking system.

In the Case of Corneal Tissue, No Public Health Threat Exists:

The FDA fails to demonstrate any compelling public health threat or need to justify the imposition of a broad regulatory approach for all tissue to include human corneal/eye tissue. **Zero transmission of systemic infectious disease in over 560,000 consecutive corneal transplants does not constitute a public health threat.**

The Present Regulatory System Provides Sufficient and Effective Oversight:

1) All U.S. eye banks are subject to present FDA regulation pursuant to part 1270 relative to HIV and hepatitis screening and testing procedures. It is misleading to allow the public to believe there are not universal standards in place, when clearly there are for HIV and hepatitis.

2) The FDA currently inspects eye banks for compliance with part 1270.

3) Should public health problems be generated from a certain eye bank, the FDA has other enforcement powers to call upon.

4) In the private sector, the EBAA provides a self regulated accreditation program for member banks. There is one eye bank operating outside the EBAA system in the State of Florida. This Florida eye bank is inspected and monitored for quality compliance under Florida State law, which has incorporated the EBAA's standards by reference.

5) The U.S. has a well defined tort system in place through its courts. Scientifically-based standards adopted by accrediting bodies would be used to define the standard of medical practice. If a bank were to significantly deviate from a community adopted standard, this standard would be referenced in a malpractice proceeding.

The EBAA believes there is sufficient oversight of the present eye banking system. Adding new broad-based regulatory requirements will not improve a 100% safety record. In fact, generic and broad-based safety requirements, inclusive of almost all types of human tissue used in transplantation, will replace the value of tissue specific safety requirements already developed and peer reviewed by specific tissue communities. This creates a situation where safety is diminished in certain communities leaving the transplant population more vulnerable to disease transmission or other quality problems.

FDA's Economic Impact Estimates Are Significantly Understated:

Human corneal tissue is a donated human gift. Under Public Health statute (P.L. 98-504; 42 USC 273 et seq., the National Organ Transplant Act of 1984) corneal tissue cannot be purchased or sold. Only the costs of acquiring tissue are reimbursable. As noted earlier, all eye banks are 501 (c)(3) organizations.

A great deal of tissue is necessarily lost throughout the medical screening process due to test results indicating contraindication to transplant or risk factors identified during construction of a donor profile. Eye banks only invoice an acquisition fee for a cornea that is transplanted. In some instances, tissue is provided by an eye bank as a charitable service for indigent care, or for furthering the advancement of the science of sight. The donating eye bank incurs all the costs associated with the procurement and distribution of the eye tissue. While there is generally no acquisition reimbursement for this tissue, in some cases the eye bank receives nominal payment for a portion of the direct costs associated with the procurement, testing, and/or transporting the tissue. In all cases, there is a financial loss to the eye bank.

Today, we are fortunate to meet the demand for corneal tissue. Tissue shortages could result in the near future given the number of new procedures which alter the cornea to improve sight (e.g. LASIK, PRK). Such individuals cannot be donors. We must be careful not to discard viable tissue for non-scientific based concerns. Cost and access problems will result.

The EBAA has reviewed the FDA's estimated economic impact of the proposed regulations and believes them to be significantly understated. The agency states the areas likely to be affected are donor screening, donor testing, record keeping, quarantine, donor suitability determinations, donor documentation, allograft documentation, and labeling.

The FDA only estimated the time needed for one person to "compare the proposed regulations against the facility's current standards". As communicated elsewhere in our response, the EBAA takes issue with the overall necessity of the proposed regulations as well as certain specific provisions. However, if implemented in their current form, the proposed regulations would necessitate changes for every one of the operational functions identified by the FDA (listed above) and others not identified for every eye bank in the United States. The time and resources necessary to comply would not be limited to "comparing" or identifying items for compliance.

For example, any identified area for change after comparing the FDA regulations to an eye bank facility's operating standards is just the first step. Typically, management and an eye bank's Medical Director must provide oversight, direction and approval of any change. Corrective action must be promulgated. Changes in the eye bank facility's standard operating procedures must be made and implemented. Most likely forms and/or logs must be changed. The most significant amount of time and resources is related to the retraining of all affected staff and subsequent quality assurance to insure compliance.

The EBAA has not performed a cost impact study but plans to do so. The economic impact is certainly more than the FDA's estimate of $45 to $229. Unfortunately, the comment period did not provide sufficient time for a thorough cost assessment of the provisions discussed therein. One authority on eye bank costs estimated the annual impact at $10,000 to $20,000 per average eye bank.

The EBAA is particularly sensitive to cost issues since the United States Health Care Financing Administration recently sought to significantly reduce Medicare reimbursement for the cost of eye banks providing a corneal tissue for transplantation. Eye Banking, as a non-profit community, inherently provides a subsidized service. An inaccurately low estimate of the impact of any additional regulation will severely harm our community's endeavors to provide our sight restoring service to the corneal blind.

The EBAA urges the FDA to correct the economic impact of the regulation. We will be happy to assist with this effort.

EBAA Proposal to the FDA:

The EBAA respectfully requests relief from the imposition of additional broad regulatory requirements established under this proposed rule for human eye tissue until a public health threat is founded. Specifically, the EBAA asks that banked human eye tissue be characterized as "Allogeneic banked human eye tissue" and that banked human eye tissue be subject to no "new" systemic-infectious disease requirements until a public health threat and need is demonstrated. Instead of being subject to unnecessary, broad-based regulatory requirements that diminish peer-reviewed tissue specific standards, the EBAA would support a mandatory reporting requirement for the transmission of systemic infectious disease through corneal transplantation.

The EBAA supported the registration provisions proposed in the Federal Register, May 14, 1998, the "Establishment, Registering, and Listing for Manufacturers of Human Cellular and Tissue-Based Products." As noted above, we would also support mandatory reporting of systemic infectious disease transmission. This requirement, coupled with mandatory registration, would provide a data collection vehicle to assess the need for additional government oversight. At this juncture, the Association believes this would be a prudent approach.

Specific Issues Contained in the Proposed Rule:

The attached pages (Attachment I, pages 1-9) address certain subject matter contained in the proposed rule. As you will note, the EBAA believes the most important issues raised in the proposed rule are not appropriate to the eye banking model. The provisions required in the proposed rule will add significant costs without the benefit of additional safety, and diminish quality standards developed by the community for tissue used in corneal transplantation procedures. In sum, the FDA could foster quality problems in a community where none have existed for over 13 years.

We appreciate the opportunity to comment on this proposed rule and hope that you find our arguments compelling. Please know that the EBAA is available to respond to any additional questions.

Sincerely,

Patricia Aiken O'Neill, Esq.
President/CEO

Enclosures